Child's Nervous System (2020) 36:241–250
https://doi.org/10.1007/s00381-019-04425-4

INVITED PAPER

Do junctional neural tube defect and segmental spinal dysgenesis have the same pathoembryological background?

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Received: 11 August 2019 / Accepted: 29 October 2019 / Published online: 10 December 2019

Abstract

Introduction Junctional neural tube defect (JNTD) is a recently introduced form of congenital spinal dysraphism that is characterized by functional disconnection between the primary and secondary neural tubes. The upper and lower cords appeared to be connected by a non-functioning band-like structure. JNTD is suspected to arise from a developmental error not corresponding to either primary or secondary neurulation, but rather between the two neurulation processes. On the other hand, segmental spinal dysgenesis (SSD) is an older entity of spinal anomalies in which a segment of the spine and spinal cord does not develop properly. The anomaly had been noted for the bony abnormality, as it is the most prominent feature. Based on the recent encounter of two cases resembling both entities, we sought the possibility that the two diseases may have the same pathoembryogenesis.

Methods and results Based on the impression that the two entities share important features, we compared the details of the two anomalies. First, our two recently encountered cases of JNTD were described. Second, previous reports of SSD were comprehensively reviewed. The two cases had the essential anomaly of the neural structures satisfying the definition of JNTD, as well as the elaborate spinal deformity as seen in SSD. In the previous literature on SSD, it was recognized that in addition to the bone anomaly, disconnected spinal cord was present. Hence, the two entities seem to have many similar clinical and neuroimaging features. The dysgenic spinal level is similar, and the disconnection between the primary and secondary neural tubes is found in the two diseases. The two neural tubes are connected by a band-like structure, with severe stenosis of the spinal canal at the level of the band. Both entities show segmental anomalies of the vertebrae in the thoracolumbar region, especially in the posterior element. Although the extent of shared features seems high, the previously suggested hypothetical pathoembryogenesis of SSD did not involve the process of junctional neurulation. We suggest that SSD shares the same origin as JNTD, and the bony abnormality may be a secondary phenomenon to the core error during neural tube development.

Conclusions We propose that JNTD and SSD may be the same entity, originating from an error during junctional neurulation. As there is controversy regarding the treatment strategy for both entities, unified accumulation of clinical experience and analysis may help improve the management of patients.

Keywords Spinal dysraphism · Neural tube defects · Segmental spinal dysgenesis · Junctional neurulation · Junctional neural tube defect

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Introduction

Recent case reports on congenital spinal anomalies introduced a new disease entity called junctional neural tube defect (JNTD) [1–3]. The most distinguishing feature was the individual formation of the primary and secondary neural tubes which was physically far apart, only connected by a thin, non-functioning band. Upper and lower segments of corresponding spinal cord appeared to have relatively normal structures. Hence, although without any supranuclear control from the brain, the lower spinal canal maintained a functional local loop of motor response. In reported cases [1–3], most affected vertebral segments ranged from T11 to L2. The patients showed various degrees of neurological deficits such as foot deformity, and motor and sensory deficits of the lower extremities according to the corresponding dysgenic spinal cord level, as well as hypertonic sphincter, urinary and fecal incontinence, or reflux with renal injury. Progressed scoliosis was shown at older ages.

On the other hand, segmental spinal dysgenesis (SSD) is an older entity of a rare congenital spinal anomaly in which a segment of the spine and spinal cord does not develop properly. It was first reported in 1852 and was then defined as a separate entity in 1988 [4], mainly interested by orthopedics due to the impressive anomaly of the bone. Most of the reports to follow were clinically focused on the bony abnormality and the orthopedic management [4–8]. In previous reports, the most affected vertebral segments ranged from T10 to L2 [9–14]. The disease was later described as focal agenesis or dysgenesis of the spine with a focal abnormality of the underlying spinal cord and nerve roots [4, 15].

The two anomalies seem to share similar clinical, radiological, and surgical features suggesting the possibility of a common pathoembryogenesis. In other words, JNTD may have focused on the neural component, whereas SSD only emphasized the bone component of an anomaly derived from the same error during development. Supporting the hypothetical concept, we have encountered two cases which showed both the typical morphology of the spinal cord of JNTD and also the spinal deformity of SSD. Here, based on the clinical observation of the two cases and review of the previous literature on SSD, we propose that the malformation of the cord during junctional neurulation is the core pathoembryologic error for both JNTD and SSD.

Clinical features of our two patients

Patient 1

Patient 1 was a 6-month-old female (Table 1). She visited our hospital due to a spinal deformity that was noted on prenatal ultrasonography, as well as an elongated gluteal fold and flat buttock (Fig. 1-A). Motor function corresponding to below the

Table 1 Summary of patients 1 and 2

Case	Age	Sex	Cutaneous sign	Presenting symptom	Spinal deformity	Level of caudal end of upper spinal cord/upper end of lower spinal cord	Motor function	Sensory function	External anal sphincter function	Kidney USG or urodynamic study
1	6 months	F	Sacral dimple	Paraparesis, primary urinary and fecal incontinence	Thoraco-lumbar vertebral segmentation failure	T10–11/L2	Bilateral weakness (motor Gr II) caudal to L2; spasticity	Decreased response to painful stimuli in lower limbs	Decreased anal tone, decreased voluntary contraction	Incompetent bladder neck, high PVR
2	7 years	F	None	Scoliosis, paraplegia, primary urinary and fecal incontinence, recent UTI	Thoraco-lumbar vertebral segmentation failure	T11/L3	Bilateral weakness (motor Gr II ~ III) caudal to L2; spasticity	Hypesthesia in L1–3, anesthesia below L3	Decreased anal tone, no voluntary contraction	Low bladder compliance, IDC, DSD, VUR, hydronephrosis, diffuse bladder wall thickening, bladder wall distortion

DSD detrusor sphincter dyssynergia, *IDC* involuntary detrusor contraction, *PVR* post voiding residual urine, *USG* ultrasonography, *UTI* upper urinary tract infection, *VUR* vesicoureteral reflux

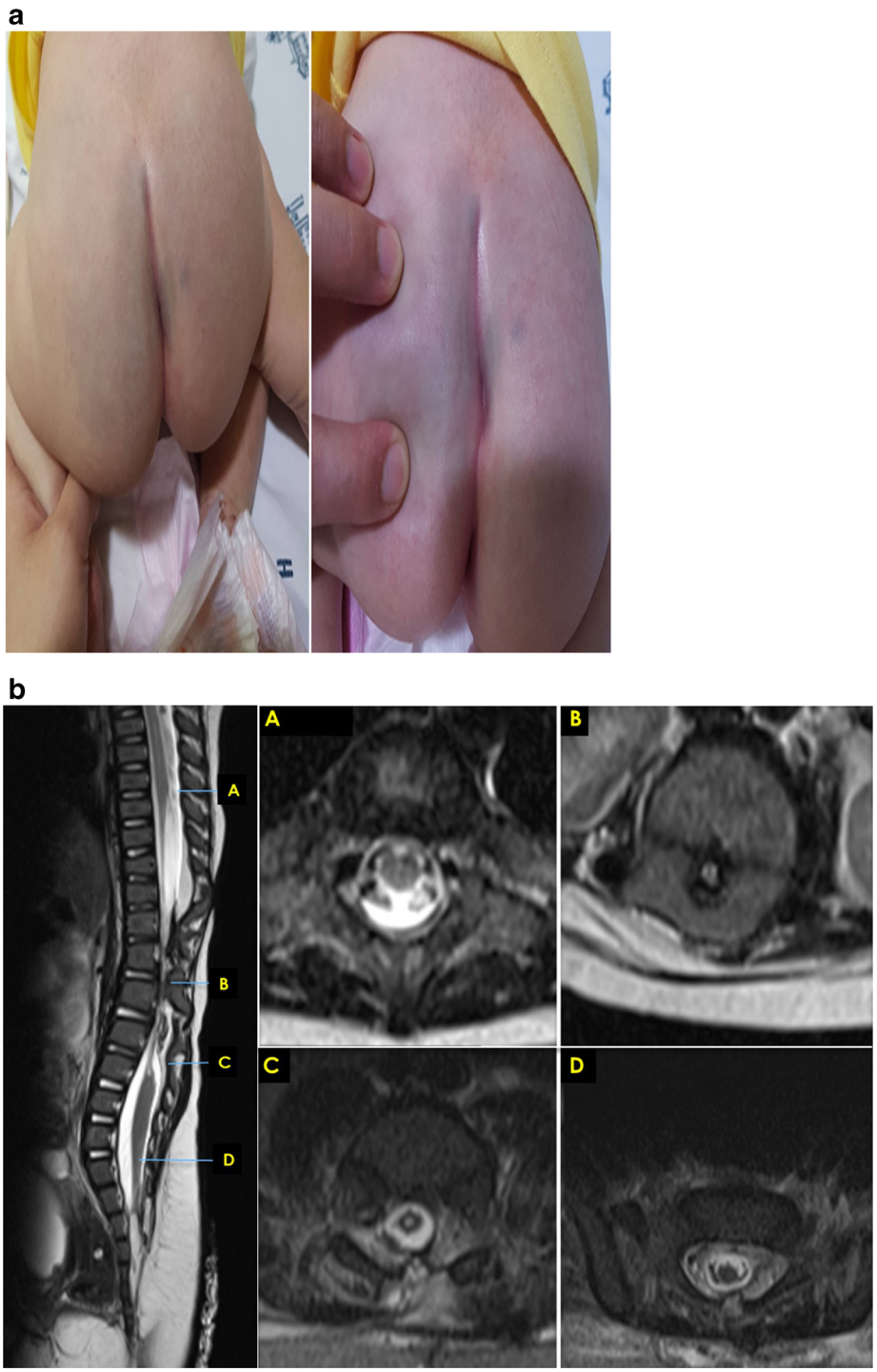

Fig. 1 Images of patient 1. A. The gross photographs of the lower back showing elongated gluteal fold. B. Preoperative MRI. Sagittal images (left) with corresponding axial images (right, A–D). (A) Upper spinal cord appeared normal in the mid-thoracic level. The spinal cord tapered into a thin band at T10. (B) The thin band continued between T10 to L2 with severely narrowed spinal canal and abnormal posterior arch of the spine. (C) The band widened into the form of a relatively normal-looking spinal cord and a conus from L2 and downward. (D) The level of the conus was low at S2 and associated with a fatty filum. C. Preoperative CT. 3D-reconstructed posterior view (left), sagittal image (middle) with corresponding axial images (right, A–D). (A) Slightly dysplastic vertebral body was shown in lower thoracic spine. The spinal canal was preserved. (B, C) There was severe spinal canal stenosis from T10 to L1 level. Dysplastic vertebral body was posteriorly displaced. The posterior elements of the spine were maximally affected, causing narrowing of the spinal canal. (D) Spinal canal widened again from L2 spine, but the posterior elements were still dysplastic. D. Intraoperative microscopic photographs. (A) At L2 level, durotomy was performed and the spinal cord was exposed. The thin band (arrowhead) was seen which widened into a rather "normal-looking" cord (asterisk) at the caudal portion. A set of normal-looking rootlets (arrows) were seen exiting from the "widened" portion of the cord. (B) L5–S3 level was exposed to perform untethering of the caudal lipoma (asterisk). After untethering, sacral rootlets (arrows) were found

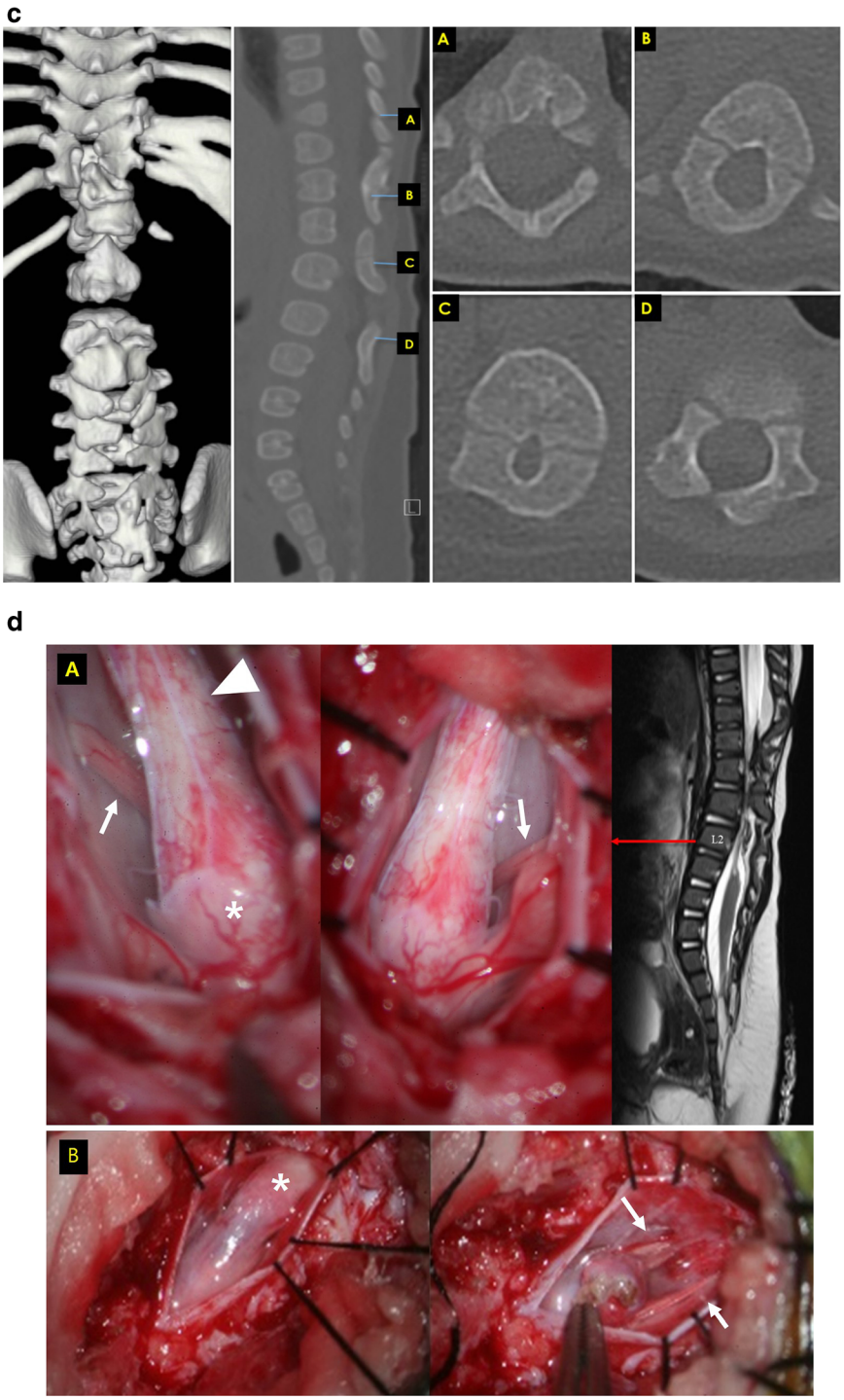

Fig. 1 continued.

L2 segment was compromised. She also showed decreased response to pain in both legs.

Preoperative spinal magnetic resonance imaging (MRI) showed that the spinal cord tapered into a thin band at the T10 vertebral level, and the thin band was present from T10 to L2. The band widened into the form of a relatively normal-looking spinal cord and a conus from L2 and downward. The level of the conus was low at S2 with full sets of normal-looking nerve roots on each side and a caudal lipoma was present (Fig. 1-B). Computed tomography (CT) demonstrated posterior vertebral segmentation anomalies in T9–S4 with severe spinal canal stenosis from T10 to L1 (Fig. 1-C).

On the urodynamic study (UDS), the post void residual (PVR) volume was 40 cc, and continuous leakage was

present. There was no vesicoureteral reflux (VUR) or detrusor sphincter dyssynergia (DSD). The preoperative motor and sensory nerve conduction study showed no abnormalities, and electromyography (EMG) showed a reduced interference pattern in the abductor hallucis muscle.

We decided to surgically decompress the severely collapsed central canal and untether the caudal lipoma. Laminectomy from T11 to L2 was performed only to find complex abnormal vascular structures in the epidural space of T11 to L1, causing profound bleeding. Therefore, the dura was not opened at the T11 to L1 level. Durotomy was performed only at the L2 level where the thin band portion of the spinal cord was seen, which widened into a rather "normal-looking" cord as expected on the MRI. A set of normal-looking rootlets were seen exiting from the "widened" portion of the cord (Fig. 1-D). Lastly, untethering and resection of the caudal lipoma was performed.

For intraoperative monitoring (IOM), we checked the EMG, motor evoked potential (MEP), somatosensory evoked potential, and bulbocavernosus reflex. The amplitude of lower extremity transcranial MEP was reduced to 0% of its baseline with the stimulation threshold 250 μV. When direct stimulation was performed with a concentric bipolar probe (spinal cord (10 mA) and nerve roots (2 mA)), the thin, connecting band region showed no response, whereas the normal-looking lower spinal cord and the set of nerve roots showed small, irregular EMG responses (Fig. 1-D (A)). Direct stimulation of the rootlets found at the location of the caudal lipoma (tip of conus) produced EMG signals of ankle and toe movements, although the patient did not have any voluntary motor function (Fig. 1-D (B)). The IOM findings showed the functional disconnection at the level of the junctional neurulation.

There were no neurological changes after the operation. She suffered from several urinary tract infections (UTIs), although no definite DSD was revealed in the follow-up UDS. At the last follow-up (28 months of age), the motor power below the knee was still grade II and showed severe spasticity of lower extremities. She had consistent urinary incontinence and leakage.

Patient 2

Patient 2 was a 7-year-old girl from a foreign country. She was first operated on when she was 1 month old. The parents recalled her diagnosis as "myelomeningocele," but the detailed history and operation record were not available. Due to kyphosis and scoliosis, multilevel lumbar instrumentation was performed at 1 year and 5 years of age in different countries.

She visited our hospital due to progressive neurogenic bladder and bilateral hydronephrosis. At the time of the visit, she was wheelchair bound. The motor powers of all muscles corresponding to levels below L2 were grades II to III. She had been performing clean intermittent catheterization and stimulated defecation. Due to progressive neurogenic bladder, she showed signs of deterioration of renal functions. The serum level of creatinine was 4.3 mg/dL (normal range, 0.5–1.0 mg/dL). She had suffered from numerous UTIs.

Preoperative spinal MRI demonstrated hypoplastic thoracolumbar vertebrae with kyphotic curvature with multilevel instrumentation. The upper spinal cord terminated at the T11 vertebral level, with a thinned connecting band-shaped spinal cord from T11 to L3. The normal-looking lower spinal cord appeared at the L3 level with low-lying conus at S2. The axial image revealed a set of normal-looking nerve roots on each side (Fig. 2). The shape of the posterior neural arch at the level of band-shaped spinal cord was closed and was not "posteriorly open" as seen in typical myelomeningocele cases.

UDS revealed low bladder compliance with involuntary detrusor contraction and DSD with substantially increased bladder tone. On the preoperative electrophysiological study, there was bilateral chronic lumbosacral polyradiculopathy at and below the L2 level. Partial rhizotomy of the ventral and dorsal roots was performed to relieve the spasticity of the bladder and prevent further renal injury. Although the spasticity of lower extremities seemed to improve after the operation, low compliance and overactivity of the bladder with DSD was still noted on the UDS performed 8 months after the operation.

Review of previous reports on SSD

Faciszewski clarified the criteria for SSD: local stenosis and deformation of the spinal canal with an osseous ring around the canal at the level of dysgenesis; affected vertebral bodies with a tendency to be displaced posteriorly; lack of neurocentral junctions, pedicles, spinous and transverse processes, nerve roots at the level of the stenosis; lack of osseous anomalies caudal to SSD [5]. It usually involves the thoracolumbar or lumbar spine. The spinal cord at the level of abnormality was thinned or indiscernible, and a bulky, low-lying cord segment was present caudal to the focal abnormality [4, 15]. Patients with SSD often suffered from progressive spinal deformity of kyphosis with gibbus apex and showed neurological dysfunctions such as lower extremity weakness and neurogenic bladder [14].

There are abundant case reports of SSD with much longer periods of follow-up compared with JNTD. Among the numerous reports, six reports with long-term follow-up and detailed information on the clinical and imaging features available are summarized in Table 2. The case of a 2-month-old girl is a good example of a typical SSD (Tortori-Donati et al. 1999 in Table 2) [14]. Her lateral spine plain radiograph showed the anomaly of L2 vertebra with severe kyphosis. The "upper" cord, which ended at the midthoracic level, and the bulky low-lying "lower" cord located below L3 were noted on the MRI. The two separate cords were connected by a thin band

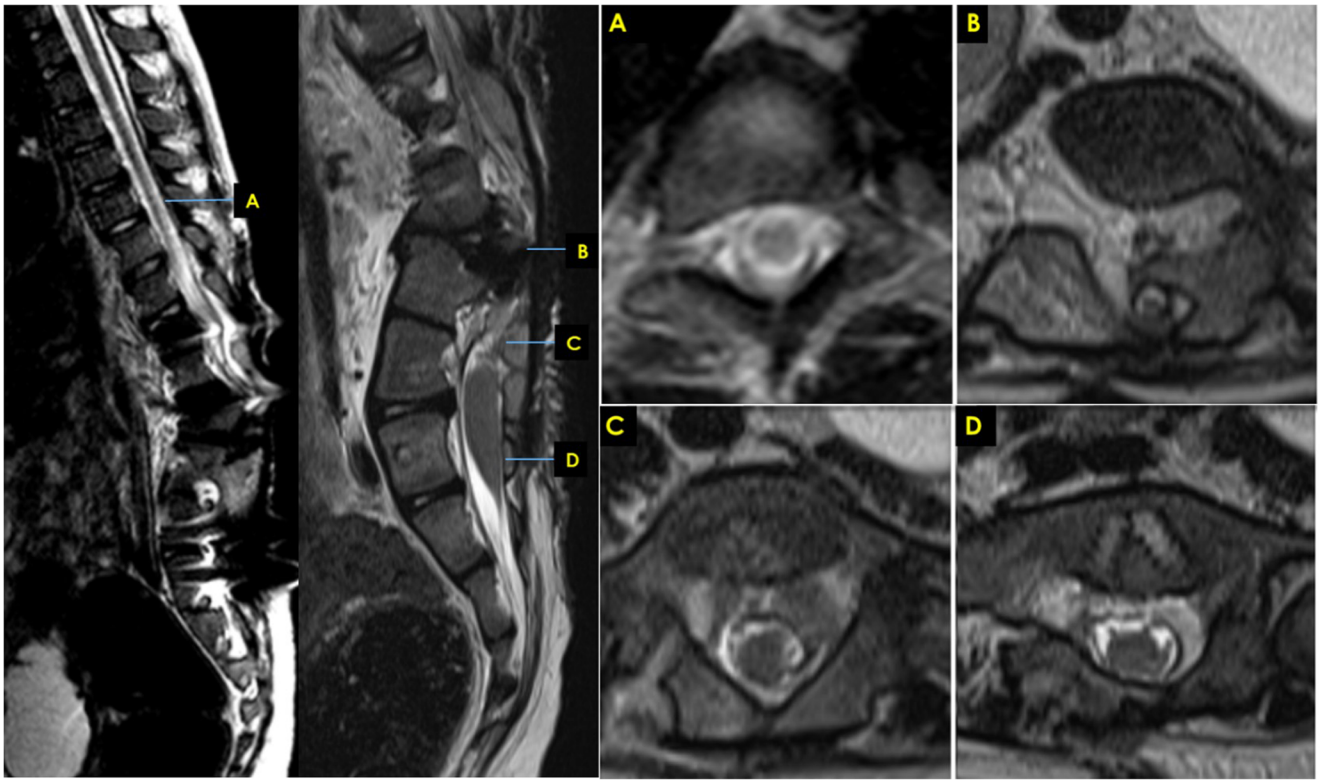

Fig. 2 Images of patient 2. Sagittal images (left, middle) with corresponding axial images (right, A–D) showing hypoplastic thoracolumbar vertebrae with kyphotic curvature with multilevel instrumentation. (A) The upper spinal cord terminated at the T11 vertebral level. (B) Thinned connecting band-shaped spinal cord was present between T11 and L3. (C, D) Normal-looking lower spinal cord was widened again at L3 spine, and the conus was low lying at S2 with a normal looking filum terminale

(Fig. 3-A). Clinically, the patient had a cutaneous stigmata of hairy tuft. She was paraparetic and suffered from neurogenic bladder and urinary incontinence.

Another case presented 13 years of follow-up for an SSD patient (Bristol et al. 2007 in Table 2) [9]. She showed a palpable bony defect at the thoracolumbar junction at birth. The spinal cord tapered severely at the thoracolumbar junction, widened again caudal to L3, and was tethered to the sacrum (Fig. 3-B). She also underwent a spinal operation for decompression of severely compressed spinal cord. She had been paraplegic since birth and was unchanged at age 15 and suffered from neurogenic bladder with frequent bladder infections.

Although there was a case of cervical SSD, there was a lack of evidence whether the case was an actual SSD [15]. This study reported on four cases, one of which was in the cervicothoracic region. However, for the cervical case, only CT image was presented, and no description of the spinal cord was available.

Discussion

JNTD and SSD share many essential radiological and clinical features. Some of the JNTD cases, including the two cases presented in this study, had elaborate anomalies including the vertebral body and posterior elements indistinguishable from SSD. Almost all of the typical SSD cases were revealed to have spinal cord anomalies typical of JNTD. Most importantly, the primary and secondary neural tubes are physically apart, only connected by a band-like structure, with severe stenosis of the spinal canal at the level of the band. The lower spinal segment below the bony anomaly seems to have somewhat normal-looking structures. Furthermore, the dysgenic spinal level is similar in the two diseases: lower thoracic and upper lumbar spine [1, 3, 10–12, 16–21]. It seems that JNTD and SSD may have originated from the same error during the development of the spinal cord.

Embryology

Along with the recent clinical interest in the anomaly with the unjoined primary and secondary neural tubes, the transitional process between the two neurulation processes was elucidated as a topic of basic developmental research by Dady et al. [22]. They defined the junctional neurulation as a distinctive process from primary and secondary neurulation. Using chick embryo models, they explored the molecular and cellular bases of junctional neurulation emphasizing topological continuity between the primary and secondary neural tubes. The

Table 2 Summary of previous reports on SSD

Authors	Age	Sex	Cutaneous sign	Presenting symptom	Spinal deformity	Level of caudal end of upper spinal cord/upper end of lower spinal cord	Motor function	Sensory function	External anal sphincter function	Kidney USG or urodynamic study	Surgical treatment
Tortori-Donati et al. [14]	1 month	F	Angioma without open defect	Equinovarus feet, deformed lower limbs, horseshoe kidneys, spastic paraplegia, clonus, reduced tendon reflexes	Hypoplastic L3 and deformed L4, partial sacrococcygeal agenesis	T9–10/L4	Spastic paraplegia	N/A	N/A	Neurogenic bladder	None
Tortori-Donati et al. [14]	2 months	F	Hairy tuft without open defect	Equinovarus feet, deformed lower limbs, spastic paraplegia, clonus, reduced tendon reflexes	Severe hypoplasia of posterior arch and posterior dislocation of L3 VB, butterfly vertebrae, T11–12	T10/L3	Spastic paraplegia	N/A	N/A	Neurogenic bladder	None
Desai et al. [11]	4 years	F	None	Spastic paraplegia, brisk knee and ankle jerks, urine and stool incontinence	Wedged shape of T7 vertebral body, block vertebrae of T8–9	T8/L1	Spastic paraplegia	Hypesthesia and hypoalgesia below T6	N/A	Bilateral hydronephrosis	None
Ofiram et al. [13]	2 months	F	N/A	Left clubfoot	Dysplastic L2, aplastic T11–L1	T10–11/L4	Left. hip flexor Gr IV, others intact	Intact	N/A	DSD without incontinence	Posterior fusion
Bristol et al. [9]	15 years	F	None	Palpable bony defect at T-L junction, purposeful movement of the hips	Dysplastic L3–4	T12–L1/L3	Paraplegia	Minimal withdrawal to pain in the lower extremities	Intact	Neurogenic bladder with frequent infection	Posterior decompression
Morell et al. [12]	2 years	M	N/A	Gibbus deformity at birth, weak ankle dorsiflexion and plantar flexion	Small L1 hemivertebrae only consisting of a lamina, bullet-shaped L2 vertebrae, severe central canal stenosis and anterolisthesis of L1	T11–12/L4	Both hip flexors, extensors Gr IV, both knee flexors, extensors Gr III	Withdrawal from painful stimuli	Intact	Required catheterization	L1, 2 vertebral column resection, T12-L3 posterior instrumentation
Cacciola et al. [10]	15 years	F	N/A	Bilateral club foot, knee and hip dysplasia, progressive weakness and pain in lower limbs, loss of bladder control	Vestigial L3, 4 VB, sacralized L5	L1–2/S1	Both hip flexors Gr II, knee extensors Gr IV–	Intact	N/A	Reflex in continence, detrusor hyperreflexia	Posterior decompression, filum resection, multiple instrumentation

N/A not available, *DSD* detrusor sphincter dyssynergia, *USG* ultrasonography, *VB* vertebral body

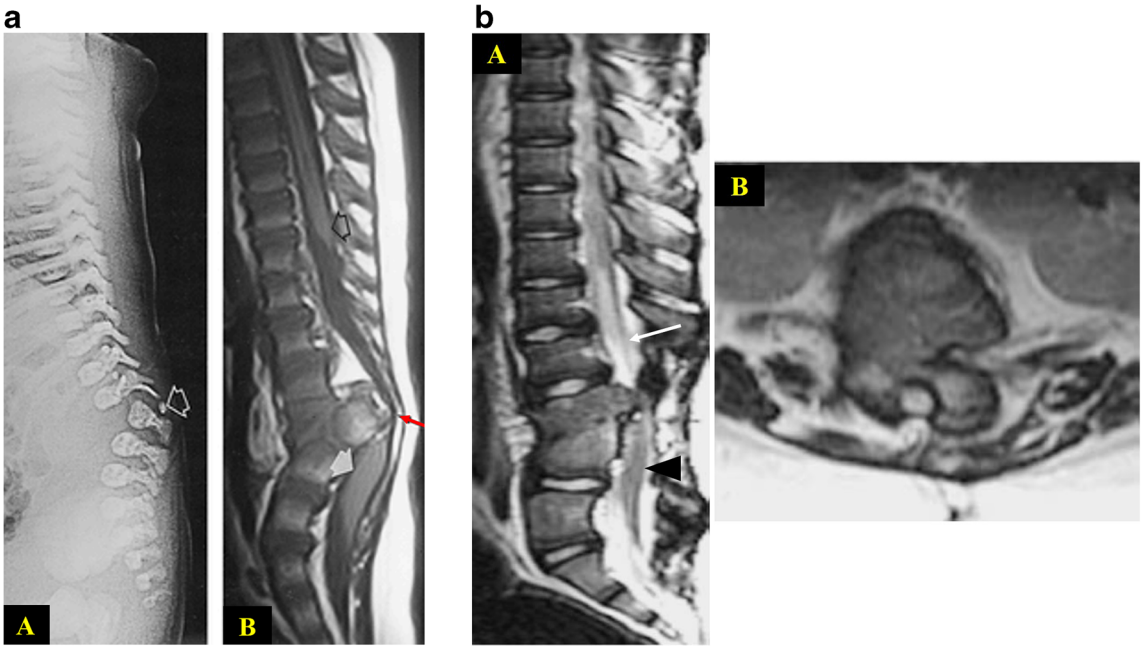

Fig. 3 Images of two previously published SSD cases. **a**. (A) Severe kyphosis (empty arrow) at L2 is noted on the plain radiograph. (B) On the MRI, the upper cord (empty arrow) tapers into a thin band (red, thin arrow) in the midthoracic region. The thin band connects the upper spinal cord to the lower spinal cord (filled arrow) which appears at L3. Reprinted from Tortori-Donati P, Fondelli MP, Rossi A, Raybaud CA, Cama A, Capra V (1999) Segmental spinal dysgenesis: neuroradiologic findings with clinical and embryologic correlation. *Am J Neuroradiol* 20:445–456, with permission of American Society of Neuroradiology. **b**. (A) Fused bony anomalies of the lower lumbar region are shown in the sagittal MRI images. Thin band (arrow) is noted to connect the upper spinal cord to the lower spinal cord (arrowhead). (B) Dysplasia of the posterior element of the spine and narrowed spinal canal are seen. Reprinted from Bristol RE, Theodore N, Rekate HL (2007) Segmental spinal dysgenesis: report of four cases and proposed management strategy. *Childs Nerv Syst* 23:359–364, with permission of Springer Nature

region (coined as "node-streak border (NSB)") between the caudal lip of Hensen's node (caudal neuropore) and the rostral end of the primitive streak was elucidated in depth [22]. NSB was morphologically continuous with the primary neural tube but showed neurulation activity before the notochord formation, which is completely different from the primary neurulation. It was shown that this region was populated by two different group of cells: dorsolateral versus ventromedial. The dorsolateral cell groups were Sox2 (+) and seemed to contribute to the primary neurulation, whereas ventromedial cells were Sox2 (−) and formed the secondary neural tube. Hence, NSB was the region of junctional neurulation, functionally and spatially connecting the primary and secondary neural tubes. By further tracking the fates of the cells in NSB, it was found that the junctional region encompasses the entire thoracic and upper lumbar regions by vertebral and spinal cord levels in the chick. This area corresponds to approximately the thoracolumbar region in humans, providing a fair rationale for the "high" position of the lesion in the JNTD or SSD (up to mid-thoracic to lower lumbar by spinal cord level which is higher in vertebral level) in contrast to the traditional concept that the junction between the primary and secondary neural tubes is at the lumbosacral region. The high location of upper extent of junctional neurulation also explains the involvement of low thoracic or lumbar area in some cases of caudal agenesis, a representative disorder of secondary neurulation. Additionally, the degree of dysgenesis and the clinical symptoms could be variable according to affected time and extent of junctional neurulation.

As the physical and functional disconnection between the primary and secondary neural tube has been described as the essential key feature of JNTD, it was proposed that an error during junctional neurulation may bring about the distinct morphology. The main player of the anomalous formation in JNTD has been the neural tube. On the other hand, the dysgenic vertebral bone has been the "proper" anomaly in SSD and several hypotheses have been proposed regarding its patholoembryologic mechanism. The most commonly mentioned idea postulates the chordomesodermal cells as the main player in the pathoembryogenesis [4, 19, 23, 24], stating that various errors during gastrulation which end up in the reduction of chordomesodermal cells will result in the malformation or near absence of the spinal column, spinal cord, and nerve roots. In other words, the anomalous or absent chordomesoderm will disturb the development of the somites, and as the notochord acts as a neural inducer, subsequent neural plate formation will also be altered. Another frequently mentioned mode of mechanism was vascular injury, based on an autopsy study in which the absence of anterior spinal artery in the area of the vertebral dysgenesis was documented [8, 25]. However, the presence of an "intact" or "thick" spinal cord below the level of the dysgenesis and also the lack of

ischemic changes in the histology decreased the credibility of the vascular hypothesis.

Although each of the two hypotheses seems to have sound arguments, at least two features seem to favor the perspective that the aberrant neural tube formation may be the main anomaly and the bony anomaly is a secondary phenomenon of the neurulation error. First, the level of the anomaly (almost always in the low thoracic and upper lumbar area, sparing the primary neurulation region) should be noted. Because the notochord acts as the neural inducer only during the primary neurulation, the explanation that the spinal cord anomaly is a secondary phenomenon due to the abnormal chordomesodermal cells seems less likely. Second, despite the profound kyphosis in some cases, the vertebral body is usually spared, and the posterior elements of the spine are mostly involved. This result may be interpreted as the timing of the error is around the time of neural tube formation and the development of the posterior arch of the spine, which occurs well after the time of induction of the neural tube by the notochord [25]. In this perspective, the more "prominent" anomaly of the vertebral bone actually seems to be a secondary phenomenon, resulting from the failure in the unification of the primary and secondary neural tubes. In other words, because of the poorly developed cord (the thin band), the neural arch was consequently formed abnormally with the fusion and faulty delineation of the spinous process, laminae, and pedicles. Hence, the term "junctional neural tube defect" more appropriately describes the essential features and pathoembryogenesis of the anomaly than does "segmental spinal dysgenesis," which focuses on the bone.

Unsettled issues regarding treatment strategy

Several issues remain regarding the treatment of JNTD and SSD, as there has been confusion among previous reports. First, the necessity of spinal cord decompression has been questioned, as a pronounced "improvement" in neurological function is almost never seen. Furthermore, no reports on definitely "progressive" neurological deficit during follow-up has been found [4, 5, 7, 9–13, 15, 16, 21]. Rather, the neurological deficits were present from the initial diagnosis and were stable throughout the disease course. A few cases in which worsening of neurological status was found were speculated to be caused by progressive scoliosis or tethering from the low-lying conus [8, 9, 14, 16]. Therefore, the severe compression of the spinal cord may actually have no effect on the neurological function with or without decompression. The idea that surgical decompression may not be necessary can also be reasoned by the hypothetical pathoembryogenesis, in which the failure of the joining of the primary and secondary neural tubes with subsequent formation of bone around the thinned band is the key, not the bony stenosis compressing the spinal cord. The "left over" junctional neural tube is actually the result of the failure and is therefore probably poorly functional or non-functional and may not be subject to dysfunction caused by physical compression. Hence, it seems likely that surgical decompression of the spinal cord is not necessary. Nonetheless, cautious examination for progressive neurological deficits should be done, as such patients may benefit from surgical decompression. Further accumulation of cases and observation of neurological function during the disease course will allow more conclusive strategies regarding this issue.

Additionally, whether untethering of the "lower spinal cord" below the band is necessary is also worth consideration. Although the definition or recognition of a "tethered cord" is not clear, if the secondary cord is suspected to have some function, it may also be safer to perform untethering, especially if the neurological deficits are partial or progressive.

Conclusion

The essential feature of both JNTD and SSD anomaly seems to be the physical and functional disconnection between the primary and secondary neural tubes. The more overt anomaly of the bone actually seems to be a secondary outcome of the neural anomaly. Although conjectural in some parts, it seems fair to propose that JNTD and SSD may be the same entity, and both diseases originate from a defect of junctional neurulation. Based on the pathoembryogenesis and clinical features, it seems neurosurgical intervention may not be beneficial in these cases.

It has been a privilege for clinicians who deal with congenital anomalies to theorize on the pathoembryology of an anomaly based on the analogy between features of anomaly and normal embryology. Nonetheless, the limitation of the study should not be overlooked, as the supposed pathoembryogenesis is speculative. Technical advances of embryological research will hopefully clarify the speculation in the future.

Acknowledgments This work was supported by the National Research Foundation of Korea (NRF) Grant funded by the Korean Government (MSIP)(NRF-2018R1A5A2025964). This work was also supported by Creative-pioneering Researchers Program through Seoul National University (SNU No. 800-20160282). This work was also supported by the Educational and Research Encouragement Fund of Seoul National University Hospital(J. Y. Lee).

Compliance with ethical standards

Conflict of interest No conflict of interest to declare.

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